HEADQUARTERS
THEATER SERVICE FORCES
EUROPEAN THEATER
Office of the Theater Chief Surgeon
(Main), APO 757

Ch Surg 710 x 444.2 28 September 1945.

CIRCULAR LETTER NO. 69

SECTION I. DIPHTHERIA.

1. GENERAL.

a. From 1 January through 24 August 1945, 1,195 cases of diphtheria and 38 deaths have been reported in US troops in this theater, the majority of these having been contracted in Germany. These cases are a direct reflection of the high incidence of diphtheria among German civilians, and continued difficulty may be expected during the coming winter months. Early diagnosis and prompt institution of specific therapy are of paramount importance. Medical officers must be keenly aware of diphtheria as a possibility and be watchful for it in all patients coming under their care.

b. This circular letter summarizes the general principles to be followed in the diagnosis, treatment, and control of diphtheria. Reference is made to paragraphs 14 and 15, Section IV, AR 40-210, 25 April 1945; to paragraph 5, TB MED 47, 28 May 1944; and to TB MED 143, February 1945. Where differences occur between procedures outlined in this directive and those in TB MED 47 and in TB MED 143, the provisions of this directive will be followed.

2. DIAGNOSIS.

a. The early clinical diagnosis in non-fulminating cases may be extremely difficult. One cannot depend entirely on the presence of the typical membrane, the appearance of which may be delayed.

b. Swelling and edema of the neck have been common findings in patients in this theater.

c. The possibility of cutaneous diphtheria must be borne in mind (see TB MED 143, February 1945).

d. A single negative nose and throat culture does not exclude diphtheria and even repeated cultures may be negative.

e. There is evidence that parenteral penicillin, and perhaps also sulfonamides, may lead to negative cultures. Nose and throat cultures must be taken before these agents are administered.

f. Two throat swabs and one nasal swab will be taken in the case of every patient complaining of sore throat or showing a blood tinged nasal discharge and sent immediately to the laboratory.

g. The technique of swabbing is important. It will be done by a medical officer using good illumination. In the case of the throat swab, care must be exercised to swab the tonsils and crypts and the posterior pharynx, particularly any areas showing grayish or white exudate or membrane.

h. Examination of direct stained smears is unreliable both in excluding and in establishing the diagnosis of diphtheria and is not recommended for that purpose although useful in determining the presence of the organisms of Vincent's angina.

i. The technique of laboratory procedures is given in paragraph 9 below.

3. TREATMENT.

a. Antitoxin:

(1) The early and adequate use of antitoxin is of primary importance. Its effectiveness is directly related to the earliness with which it is given and therefore it must be promptly administered in all clinically suspicious cases except where marked sensitivity to horse serum exists.

(2) Dosage:

(a) 30,000 units will be given as soon as the clinical diagnosis is made.

(b) A second dose of 30,000 units will be given eight hours later.

(c) In severely toxic cases and those with extensive membranes an additional 30,000 units is advisable eight hours following the second dose.

(3) Administration will be by the intramuscular route, the lateral muscles of the thighs being the site of choice. In extremely toxic cases, the injection of the first 30,000 units by the intravenous route rarely may be necessary.

(4) All individuals will be tested for sensitivity to horse serum prior to the administration of antitoxin. Every effort will be made to desensitize those individuals found to be sensitive. Reference is made to paragraph 3, TB MED 114, 9 November 1944.

b. Chemotherapy:

(1) It must be emphasized that chemotherapy is purely subordinate to the use of antitoxin and does not replace it.

(2) Penicillin:

(a) This agent aids in the rapid improvement of the clinical condition and when administered during the first week of the disease reduces the incidence of carriers. A minimum initial dose of 30,000 units will be given followed by 20,000 units every three hours for five days.

(b) There is no conclusive evidence that local use of penicillin in the throat is of value.*

(3) Sulfonamides:

(a) Secondary infections with hemolytic streptococci are frequently associated with C. diphtheriae. Since this and other secondary invaders usually are sensitive to penicillin, sulfonamides are not indicated when penicillin is used. If, however, penicillin is not available, sulfadiazine should be administered.

4. CONVALESCENCE.

a. Because of the frequency of myocardial damage in diphtheria, a prolonged period of rest is essential. The following routine for convalescence is recommended:

(1) First and second weeks --

(a) Complete bed rest.

(b) Patient to be bathed and fed by nurse or attendant.

(2) Third week -- patient remains in bed but unless cardiac damage is present is allowed increasing activity in bed.

(3) Fourth week -- patient is allowed to sit up for one hour daily.

(4) Fifth and sixth weeks -- patient may be ambulatory, the number of hours and the amount of exercise being gradually increased.

b. Electrocardiograms should be taken at weekly intervals on all patients and more often when the findings are abnormal. In the presence of cardiac damage, the period of bed rest must be extended depending on the degree of involvement.

5. MANAGEMENT OF CONVALESCENT AND ASYMPTOMATIC CARRIERS.

a. The presence of C. diphtheriae after the end of the fifth week of the disease, or in an asymptomatic individual, indicates the existence of the carrier state. These individuals must be kept isolated and given suitable treatment. They may lead a normal life within the bounds of isolation. In no case should a carrier of virulent diphtheria be used as a food handler.

b. Before patients or carriers can be released from isolation, three swabs taken from the nose and throat at 48 hour intervals, followed by a fourth swab taken one week later, must be negative. Experience has shown that the taking of cultures to determine the existence of the carrier state is rarely of value prior to the third week of the disease.

c. Determination of the type of C. diphtheriae is important and virulence tests should be done. If the strain is found to be non-virulent, the patient may be released.

d. It has been definitely established that penicillin given early tends to lower the incidence of carriers. However, once the carrier state has developed, it is probable that penicillin therapy is of no value.

e. Tonsillectomy has proved to be highly effective in clearing the carrier state.

6. MANAGEMENT OF CONTACTS.

a. Contacts will be inspected by a medical officer daily for 5 days following exposure. The inspection will include examination of the throat.

b. If practicable, contacts will be excluded from food handling until shown to be free from virulent C. diphtheriae. Culturing of contacts other than food handlers is rarely indicated.

7. IMMUNIZATION.

a. Paragraph 11c of Section III, AR 40-210, 25 April 1945, provides that immunization against diphtheria may be carried out when in the opinion of the surgeon such is necessary for the prevention or control of diphtheria within the command. Reference is also made to paragraph 7c of TB MED 143, February 1945, and to paragraph 4j of TB MED 114, 9 November 1944. Toxoid causes very severe local and general reactions in such a high percentage of adults that its use in military personnel is advisable only under the most urgent conditions.

b. Where practicable, only immune personnel will be utilized in caring for diphtheria patients.

8. REPORTING OF CASES.

a. When a diagnosis of diphtheria is made, the responsible officer of the hospital or other installation involved will report it by the quickest possible means to:

(1) The commanding officer of the patient's unit, in order that careful watch may be made for additional cases.

(2) The major command headquarters having jurisdiction. (District, Air Force, Base Section.)

(3) Office of the Theater Chief Surgeon, Preventive Medicine Division, Headquarters, Theater Service Forces (Main), APO 757 (telephone: ROUNDUP 33412).

(4) The reports will include the patient's name, unit, location, date of onset, and name of reporting hospital.

9. LABORATORY PROCEDURE.

a. Cultures.

(1) Immediately upon receipt of the swabs by the laboratory, the following will be done:

(a) One throat swab will be used for inoculation of:

1. A section of a blood or serum tellurite plate,*

2. A section of a blood agar plate.

3. A Loeffler slant.

(b) Similar inoculations will be made with the nose swab.

(c) All cultures will be immediately incubated at 36° C. to 37° C.

(d) The second throat swab is used to prepare a direct smear which should be fixed by heat, stained with methylene blue or dilute fuchsin, and examined for the organisms of Vincent's angina.

(2) The presence of hemolytic streptococci will be evident on the blood plate after 18 to 24 hours' incubation. It is essential that the blood agar which is used should have been previously tested and found suitable. Moreover, since certain hemophilus organisms may yield colonies indistinguishable from beta streptococci, a gram stain should be done for confirmation.

(3) The diphtheria bacillus should be evident both on the tellurite plate and the Loeffler slant in 15 to 18 hours. The tellurite medium is highly selective. Abundant confluent growth at this time will usually prove to be C. diphtheriae. In such instances, microscopic examination of the growth on Loeffler medium after staining with methylene or toluidine blue, or Albert's

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*Tellurite media is available upon requisition from the Fourth Medical Laboratory, APO 887. This media is available in limited quantities only, so that laboratories must be extremely careful to avoid waste.

stain will usually confirm the diagnosis. The morphology of the organism on tellurite is less characteristic. Polar bodies are absent or inconspicuous but it is readily possible to decide whether the growth is a Corynebacterium rather than a staphylococcus, M. catarrhalis, Friedlander bacillus, or yeast (the other organisms which may occasionally appear).

(4) Such positive findings will be reported by the laboratory to the ward officer immediately and constitute strong presumptive evidence of diphtheria. Laboratory study will be continued, however, to determine the type of the strain and its virulence.

b. Determination of Type of Strain.

(1) In Europe at the present time, about four-fifths of all cases of diphtheria are due to the mitis strain of C. diphtheriae. Most of the remainder are caused by gravis strains and a few by intermedius. Since the relation of these various types of infection to clinical severity, response to antitoxin, and sequellae is not entirely clear, every positive culture report should include a statement of the type to provide data for future analysis. The variation in morphology among these strains either on Loeffler's medium or on tellurite, and the prevalence of Hoffman's bacillus and other non-pathogenic Corynebacteria, make necessary the actual isolation in pure culture of the organism in question, and the determination of its fermentative properties as well as its virulence toward animals.

(2) Appearance on Tellurite Plates. At the end of 24 hours' incubation of the tellurite plates, mitis colonies are black, round, convex, glistening, and measure 1 to 2 mm in diameter. Gravis colonies are flat, dull, slate gray, and measure 2 to 4 mm. Intermedius colonies are pin-point in size and exhibit a rather characteristic brown color. However, atypical strains have been described and may be encountered. The Hoffman bacillus resembles the mitis colony but is generally less deeply colored and may show a definite dark center and light periphery. The majority of negative cultures at this time will show no growth whatever and can be so reported and discarded.

(3) Fermentative Properties. Smears stained with alkaline methylene blue should be examined from cultures showing growth, and colonies of Corynebacteria restreaked on ½ of a fresh tellurite plate so as to obtain definite single colonies from which pure cultures on Loeffler or brain-heart agar can be prepared. These pure cultures are used, after incubation, for inoculating Hiss serum-water sugars (glucose, saccharose and starch). The fermentation results are usually apparent in 24 hours, although it is well to defer final recording for 3 days. Glucose should be fermented by all strains, saccharose by none. Starch fermentation occurs only with gravis strains. Rarely, virulent strains

may show atypical fermentations. Non-virulent strains, though culturally and morphologically typically mitis, are frequently encountered in healthy individuals. This is reported to be rarely, if ever, the case with gravis, and information regarding the intermedius type is lacking.

c. Virulence Tests.

(1) Virulence tests are not necessary in the case of gravis strains but are important in all others.

(2) Technique:

(a) Twenty-four hour pure cultures on Loeffler's slants or brain-heart agar are suspended in saline by adding 5 cc. of sterile saline and mixing. This suspension should have a density equal to McFarland density No. 3.

(b) 0.1 cc. of this saline suspension is injected intradermally into the shaved skin of a rabbit or guinea pig (Test Injection "A").

(c) Not less than three nor more than seven hours later 0.5 to 1 cc. (depending on the size of the animal) of diphtheria antitoxin is injected intravenously into the rabbit. If a guinea pig is used, 0.5 cc. is given intraperitoneally.

(d) Immediately a second injection of 0.1 cc. of the suspension of culture is given intradermally (Test Injection "B").

(e) The test is read after 72 hours in the case of rabbits and after 48 hours in guinea pigs. A positive reaction consists of an area of erythema measuring 10 to 15 mm. in diameter with a necrotic center measuring 2 to 5 mm.

(f) If the test strain is virulent a positive skin reaction will occur at the site of test injection "A" but not at that of test injection "B". If the strain is non-virulent, both sites will show negative reactions. Not infrequently a small reaction is seen at test site "B", in which case a reaction at site "A" is without significance unless it is distinctly larger than that at "B".

(g) As a control, one strain of known virulence should be included in each series of unknown strains tested.

(h) As many as fourteen tests can be performed on a single rabbit at one time, but when once used for this purpose the animal cannot be used again for virulence tests.

SECTION II. ITEM 1605900, INFLUENZA VACCINE.

1. Subject item is expected to be received in the theater within a very short period for the vaccination of all military personnel as directed by War Department Circular 267, dated 5 September 1945. The dosage is one injection of 1 cc. influenza vaccine. It is necessary to exercise careful control in the distribution and use of the influenza vaccine supply. Quantities available are adequate only if wastage and loss are held to an absolute minimum.

2. It is desired that careful attention be given to proper storage and conservation of subject item to insure having adequate quantities on hand to cover the theater's requirements. Wastage will be held to an absolute minimum.

3. Influenza vaccine must be stored under normal temperature of 45°F. Since rail refrigeration service is not available at this time, all shipments of influenza vaccine will be made by air wherever practicable. Short hauls will be made by fastest possible motor transportation. Containers used for shipping subject vaccine will be marked "Perishable. Refrigerate under 45°F. as soon as possible. Contents 'VACCINE'".

By order of the Theater Chief Surgeon:

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